Isolation and Structure-Activity Studies of SchistoFLRFamide - like Peptides

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The sequences of two FMRFamide-related peptides from *Locusta* central nervous system have recently been determined. One peptide is identical to the previously described SchistoFLRFamide (PDVDHVFLRFamide), while the second peptide is novel and differs from SchistoFLRFamide in positions 1 and 4 (ADVGHVFLRFamide). Both are inhibitory peptides when assayed on locust oviduct; inhibiting myogenic contractions, lowering basal tonus, and inhibiting proctolin-induced contractions.

Bioassays and binding assays have shown that the His residue in the truncated analog HVFLRFamide is critical for the retention of inhibitory biological activity, whereas VFLRFamide, in which inhibitory biological activity is lost, is the minimum sequence for binding of comparable affinity to the parent compound. Substitution of His by the D-isomer or Phe produced analogs with stimulatory rather than inhibitory activity confirming the importance of the His moiety. In addition, inhibitory activity was retained when the His moiety was methylated at the N-3 position of the imidazole ring, but methylation of N-1 yielded a peptide which stimulated contractions. Inhibitory activity was further retained when N^{α}-methyl-L-His and D,L - 1', 2', 4' - triazole-3-Ala were substituted for His.

We have also described a nonpeptide mimetic analog of these receptors. Benzethonium chloride (Bztc) is an agonist of the PDVDHVFLRFamide receptors found on locust oviducts. Bztc competitively displaces [^{125}I-labelled Y^1]DVDHVFLRFamide binding to both high- and low-affinity receptors of membrane preparations and mimics the physiological effects of PDVDHVFLRFamide on locust oviduct. Bztc is therefore recognized by the binding and activation regions of these receptors. This discovery provides a unique opportunity within insects to finally target a peptide receptor for the development of future pest management strategies.